



**IN THE  
UNITED STATES OF PATENT AND TRADEMARK OFFICE**

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|----------------------|------------------------------------|
| Attorney Docket      | CELL-004CON                        |
| First Named Inventor | Henderson                          |
| Application Number   | 09/732,169                         |
| Filing Date          | December 6, 2000                   |
| Group Art Unit       | 1633                               |
| Examiner Name        | B. Whiteman                        |
| Title:               | TISSUE SPECIFIC ADENOVIRAL VECTORS |

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**DECLARATION UNDER 37 C.F.R. 1.131**

Assistant Commissioner for Patents  
Washington D.C. 20231

This Declaration with the attached Exhibits are being submitted in conjunction with the Applicants' Response to the Office Action dated August 27, 2002.

We, Daniel Henderson and Eric Shuur, being duly sworn, declare that:

We are the joint inventors of the subject matter described and claimed in the above-captioned patent application. We have read and understand the Office Action of August 27, 2002 and the references cited by the Examiner, including U.S. Patent Application no. US2001/0053768, claiming priority to U.S. Patent application no. 08/433,798, filed May 3, 1995, herein referred to as the Gregory application.

Prior to May 3, 1995 (the priority date of the Gregory application), we had formulated the conception of a tissue-specific replication-conditional adenovirus vector comprising a heterologous tissue-specific transcriptional regulatory sequence operably linked to the coding region of a gene that is essential for the replication of said vector, and the use of such a vector for the selective cytolysis of target cells. Evidence is provided by Exhibits A, B, C, D, E and F. All redacted dates are prior to May 3, 1995.

Exhibit A consists of signed laboratory notebook pages from D. Henderson, describing the conception of a "tissue-specific virus". The virus would "drive E1A with PSE [prostate specific enhancer]", and could be grown in cells to create "replication competent virus".

Exhibit B consists of signed laboratory notebook pages from D. Henderson, describing the genetic construction that would be used to create the tissue specific adenovirus. The hand-drawn figure shows the restriction sites, coding regions, and regulatory elements that are in the tissue specific virus.

Exhibit C consists of signed laboratory notebook pages from D. Henderson, showing the results of restriction digestions, and ligations, providing detailed examples of specific reporter constructs.

Exhibit D consists of signed laboratory notebook pages from D. Henderson describing strategies for construction of the constructs, by moving in the reporter genes and performing PCR on the minimal enhancer then moving in the enhancer by way of a second cloning step.

Exhibit E consists of signed laboratory notebook pages from D. Henderson, and from Gail Henderson, who was working under his direction. Included is an agenda for adenovirus constructs, and description for the construction of adenovirus constructs. The exhibit also shows diagrams of constructs in progress.

Exhibit F consists of signed laboratory notebook pages from D. Henderson describing strategies for synthesizing oligos to be used in PCR, and an updated agenda for adenovirus constructs.

From May 3, 1995 until Applicants claimed priority date of June 27, 1995, Applicants were diligent towards reducing the invention to practice, as evidenced by the attached exhibits.

Exhibit G consists of signed laboratory notebook pages from Gail Henderson, describing the growth of plasmids containing elements used in the final virus construct, the verification of structures by restriction digestion. The notebook pages are dated May 8, 1995, May 17, 1995 and May 18, 1995.

Exhibit H consists of a letter sent by Applicants' patent counsel dated June 23, 1995, in which a draft application of the patent application was enclosed.

Applicants respectfully submit that the invention set forth in the present application was conceived prior to the effective priority date of the Gregory application, U.S. Patent Application no. US2001/0053768. Applicants were diligent in reducing the invention to practice from the conception date, to the date of filing of priority application 08/495,034, on June 27, 1995.

We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Respectfully submitted,

Date: 1/24/03

D.R. Henderson  
Daniel Henderson

Date: \_\_\_\_\_

\_\_\_\_\_  
Eric Shuur